In the Claims

1-19 (canceled).

- 20 (currently amended). A method of identifying a candidate molecule for the treatment of schizophrenia, depression or bipolar disorder, said method comprising:
- (a) contacting a <u>D-amino acid oxidase (DAO) polypeptide comprising SEQ ID NO: 7DAO or</u>

 <u>DDO polypeptide</u> or a <u>biologically active</u> fragment thereof <u>that has DAO</u> enzymatic <u>activity</u> with a test compound; and
 - (b) determining whether said compound
- (i) selectively reduces the <u>enzymatic</u> activity of said polypeptide <u>or fragment</u> thereof; or
- (ii) selectively binds said polypeptide or fragment thereof; wherein a test compound that selectively reduces the enzymatic activity of said polypeptide or fragment thereof or selectively binds to said polypeptide or fragment thereof is identified as a candidate molecule for the treatment of schizophrenia, depression or bipolar disorder.
- 21 (currently amended). A method of screening for antagonists of a DAO or a DDO polypeptide, comprising the steps of:
- (a) contacting a test compound with a DAO or DDO polypeptide comprising SEQ ID NO: 7; selected from the group consisting of;
- (i) a polypeptide comprising a polypeptide encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 2 to 6, 19 and 20;
- (ii) a polypeptide comprising a polypeptide sequence selected from the group consisting of SEQ ID NOS: 7 to 10, 21 and 22;
 - (b) detecting the level of DAO activity; and

(c) comparing the activity to the activity of a control test without the test compound, whereby a decrease in the level of <u>DAO</u> the <u>DAO</u> or <u>DDO</u> activity over the control indicates that the test compound is an antagonist of DAO or <u>DDO</u>.

22-29 (canceled).

30 (previously presented). The method according to claim 20 or 21, wherein said test compound is:

(1) a compound represented by the structure:

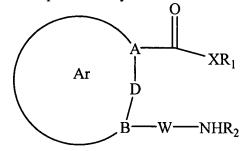
$$Ar$$
 Ar
 Ar
 R_1

- a) A is alkyl; branched chain alkyl; or cycloalkyl, any of which can be substituted with C₁-C₆ alkyl, halo, hydroxyl or amino;
- b) X is O or N;
- c) Ar is an aromatic mono-, bi- or tricyclic fused heterocyclic ring, wherein the ring is either unsubstituted or substituted in one to five position(s) with hydrogen, halogen, hydroxyl, -CN, COR₂, --CONR₂R₃, --S(O)_nR₂, --OPO(OR₂)OR₃, --PO(OR₃)R₃, --OC(O)NR₂R₃, --COOR₂, --CONR₂R₃, --SO₃H, --NR₂R₃, --NR₂ COR₃, --NR₃ COOR₃, --SO₂ NR₂ R₃, --N(R₂) SO₂ R₃, --NR₂ CONR₂R₂, --SO₂NHCOR₂, --CONHSO₂R₂, --SO₂NHCN, --OR₁, C₁-C₆ straight or branched chain alkyl or alkenyl, or C₁-C₆ branched or straight chain alkyl or alkenyl which is substituted with one or more, halogen, hydroxyl, amino, carboxy, carboxamide, nitrile, nitro, alkoxy, trifluoromethyl, sulfur, sulfonate, phosphonate, phosphate, Ar¹, N₃ or a combination thereof and wherein the heterocyclic ring contains 1-6

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heteroatom(s) selected from the group consisting of O, N, S, and a combination thereof;

- d) R₄ is H, alkyl, Ar¹, O, or a substituted alkyl;
- e) R¹ is C₁-C₆ alkyl, Ar¹, C₁-C₄ alkoxycarbonylmethyl, or a substituted alkyl;
- f) R₂ and R₃ are each independently, hydrogen, C₁-C₆ straight or branched chain alkyl or alkenyl, or C₁-C₆ branched or straight chain alkyl or alkenyl which is substituted with one or more, halogen, hydroxyl, amino, carboxy, carboxamide, nitrile, nitro, alkoxy, trifluoromethyl, sulfur, sulfonate, phosphonate, phosphate, Ar¹, or N₃; and
- g) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro, trifluoromethyl, C₁-C₆ straight or branched chain alkyl or aklenyl, C₁-C₄ alkoxy, C₁-C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the individual ring sizes are 3-7 members; and wherein the heterocyclic ring contains 1-6 heteroatom(s) selected from the group consisting of O, N, S, and a combination thereof;
- (2) a compound represented by the structure:



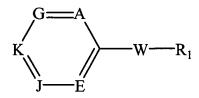
- a) A and B are carbon or nitrogen and D has 0-2 members that are carbon or nitrogen;
- b) W is $(CH_2)_n$ or a branched chain alkyl, wherein n is 0-4 and when n=0 NHR₂ is covalently bound to B;
- c) X is O or N;

- d) R₂ is H, alkyl, Ar¹, or O substituted alkyl;
- e) R^1 is C_1 - C_6 alkyl, Ar^1 , C_1 - C_4 alkoxycarbonylmethyl, or substituted alkyl;
- f) Ar is an aromatic mono-, bi- or tricyclic fused heterocyclic ring, wherein the ring is either unsubstituted or substituted in one to six position(s) with halo, hydroxyl, nitro, trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁-C₄ alkenyloxy, phenoxy, benzyloxy, amino, C₃-C₆ cycloalkyl or a combination thereof; wherein the individual ring sizes are 5-6 members; and wherein the heterocyclic ring contains 1-6 heteroatom(s) selected from the group consisting of O, N, S, and a combination thereof; and Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro, trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁-C₄ alkenyloxy, phenoxy, benzyloxy, amino, C₃-C₆ cycloalkyl or a combination thereof; wherein the individual ring sizes are 3-7

members; and wherein the heterocyclic ring contains 1-6 heteroatom(s)

selected from the group consisting of O, N, S, and a combination thereof;

(3) a compound represented by the structure:

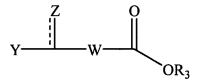


- a) A, G, K, J, E are members of a six membered carbon or heterocyclic aromatic ring, wherein the heterocyclic ring contains 1-6 atom(s) selected from the group consisting of C, N and a combination thereof:
- b) A, G, K, J, E may each independently be unsubstituted or substituted with hydrogen, halogen, hydroxyl, -CN, COR₂, --CONR₂R₃, --S(O)_nR₂, --OPO(OR₂)OR₃, --PO(OR₃)R₃, --OC(O)NR₂R₃, --COOR₂, --CONR₂R₃, --

 SO_3H , --NR₂R₃, --NR₂COR₃, --NR₃COOR₃, --SO₂NR₂R₃, --N(R₂)SO₂R₃, --NR₂CONR₂R₂, --SO₂NHCOR₂, --CONHSO₂R₂, --SO₂NHCN, --OR₁, C₁-C₆ straight or branched chain alkyl, C₁-C₆ straight or branched chain alkenyl, or C₁-C₆ branched or straight chain alkyl or alkenyl which is substituted with one or more, halogen, hydroxyl, amino, carboxy, carboxamide, nitrile, nitro, alkoxy, trifluoromethyl, sulfur, sulfonate, phosphonate, phosphate, Ar¹, or N₃;

- c) R₁ is CN, COR₂, --CONR₂R₃, --S(O)_nR₂, --OPO(OR₂)OR₃, --PO(OR₃)R₃, --OC(O)NR₂R₃, --COOR₂, --CONR₂R₃, --SO₃H, --NR₂R₃, --NR₂COR₃, --NR₃COOR₃, --SO₂NR₂R₃, --N(R₂)SO₂R₃, --NR₂CONR₂R₂, --SO₂NHCOR₂, --CONHSO₂R₂, --SO₂NHCN, SCN, COCO₂H, C₁-C₆ straight or branched chain alkyl or alkenyl, or C₁-C₆ branched or straight chain alkyl or alkenyl which is substituted with one or more halogen, hydroxyl, amino, carboxy, carboxamide, nitrile, nitro, alkoxy, trifluoromethyl, sulfur, sulfonate, phosphonate, phosphate, Ar¹, or N₃;
- d) W is N, $(CH_2)_x$, or $-NCH_2$;
- e) x=0-4;
- f) n=0-2;
- R₂ and R₃ are each, independently, hydrogen, C₁-C₆ straight or branched chain alkyl or alkenyl, or C₁-C₆ branched or straight chain alkyl or alkenyl which is substituted with one or more halogen, hydroxyl, amino, carboxy, carboxamide, nitrile, nitro, alkoxy, trifluoromethyl, sulfur, sulfonate, phosphonate, phosphate, Ar¹, or N₃; and
- h) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro, trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁-C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the individual ring sizes are 5-6 members; and wherein the heterocyclic ring contains 1-6 heteroatom(s) selected from the group consisting of O, N, S, and a combination thereof;

(4) a compound represented by the structure:



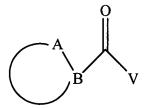
- a) $W=(CH_2)_n$;
- b) n=0-5;
- c) Z is oxygen or hydroxyl;
- d) Y= H, Ar^1 , R_4 (CH₂)_x, $R_1S(CH_2)_{x^{--}}$, $R_1SO(CH_2)_{x^{--}}$, $R_1SO_2(CH_2)_{x^{--}}$, $R_1SO_3(CH_2)_{x^{--}}$, $HNR_1SO_2(CH_2)_{x^{--}}$, $R_1R_2N(CH_2)_x$, $R_1O(CH_2)_{x^{--}}$, CF_3 , or OH;
- e) x=0-6;
- f) R₁, R₂ and R₃ are each independently hydrogen, C₁-C₆ straight or branched chain alkyl or C₁-C₆ branched or straight chain alkyl substituted with one or more halogen, hydroxyl, amino, carboxy, carboxamide, nitrile, nitro, alkoxy, trifluoromethyl, sulfur, sulfonate, phosphonate, phosphate, or Ar¹;
- g) R₄ is a halogen, CN, N₃, C₁-C₆ straight or branched chain alkyl or C₁-C₆ branched or straight chain alkyl substituted with one or more halogen, hydroxyl, nitro, alkoxy, trifluoromethyl, sulfonate, phosphonate, phosphote, Ar¹, --COR₁, --COOR₁, CONR₁R₂, CN, --NR₁, --NR₁R₂, --SR₁, --SO₂NHCN, or N₃; and
- h) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro, trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁-C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the individual ring sizes are 5-6 members; and wherein the heterocyclic ring contains 1-6 heteroatom(s) selected from the group consisting of O, N, S, and a combination thereof;

(5) a compound represented by the structure:

$$Ar^1$$
 W OH

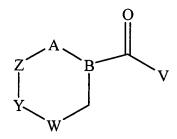
or pharmaceutically acceptable salts thereof, wherein:

- a) Y is Ar¹;
- b) Z is a carbonyl or hydroxyl;
- c) W is $(CH_2)_n$ wherein n = 0, 1, or 2; and
- d) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro, trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁-C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the individual ring sizes are 5-6 members; and wherein the heterocyclic ring contains 1-6 heteroatom(s) selected from the group consisting of O, N, S, and a combination thereof;
- (6) a compound represented by the structure:



- a) A and B taken together, form a 5-8 membered saturated or partially unsaturated heterocyclic ring containing at least one additional O, S, SO, SO₂, NH, or NR¹ heteroatom in any chemically stable oxidation state;
- b) V is O, OR_1 , NR_2 , NR_1 , R_2 , CHR_1R_2 , CH_2R_3 , CHR_3R_4 , or CH_2N_3 ;

- c) R₁ and R₂ are independently hydrogen, C₁- C₆ straight or branched chain alkyl or C₁-C₆ branched or straight chain alkyl substituted with one or more halogen, hydroxyl, amino, carboxy, carboxamide, nitro, alkoxy, trifluoromethyl, sulfur, sulfonate, phosphonate, or Ar¹;
- d) R₃ and R₄ are either halogen, C₁- C₆ straight or branched chain alkyl or C₁-C₆ branched or straight chain alkyl substituted with one or more hydroxyl, amino, carboxy, carboxamide, nitro, alkoxy, trifluoromethyl, sulfur, sulfonate, phosphonate, Ar¹, --OC(O)R₁, --COOR₁, CONR₁R₂, CN, NR₁, NR₁R₂, SR₁, SO₂NHCN, or N₃, and
- e) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro, trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁-C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the individual ring sizes are 5-6 members; and wherein the heterocyclic ring contains 1-6 heteroatom(s) selected from the group consisting of O, N, S, and a combination thereof;
- (7) a compound represented by the structure:



- a) W-Y-Z-A-B comprise a six membered saturated or partially saturated carbocyclic or heterocyclic ring, wherein the heterocyclic ring contains heteroatom(s) selected from the group consisting of -O, N, S, and any combination thereof:
- b) B is either C, CH, or N;

- c) A, W, Y, Z are each independently CH₂, CHR₃, CR₃R₄, O, S, SO, SO₂, NH, NR₁, NR₁R₂, or C=O;
- d) V is O, OR_1 , NR_2 , NR_1R_2 , CHR_1R_2 , CH_2R_3 , CHR_3R_3 or CH_2N_3 ;
- e) R₁ and R₂ are independently hydrogen, C₁-C₆ straight or branched chain alkyl or C₁-C₆ branched or straight chain alkyl substituted with one or more halogen, hydroxyl, amino, carboxy, carboxamide, nitrile, nitro, alkoxy, trifluoromethyl, sulfur, sulfonate, phosphonate, phosphate, or Ar¹;
- f) R₃ and R₄ are each independently halogen, --OC(O)R₁, --COOR₁, --CONR₁R₂, CN, --NR₁, --NR₁R₂, --SR₁, --SO₂NHCN, N₃, C₁-C₆ straight or branched chain alkyl or C₁-C₆ branched or straight chain alkyl substituted with one or more halogen, hydroxyl, nitro, alkoxy, trifluoromethyl, sulfonate, phosphonate, Ar¹, --OC(O)R₁, --COOR₁, --CONR₁R₂, CN, --NR₁, --NR₁R₂, --SR₁, --SO₂NHCN, or N₃; and
- g) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro, trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁-C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the individual ring sizes are 5-6 members; and wherein the heterocyclic ring contains 1-6 heteroatom(s) selected from the group consisting of O, N, S, and any combination thereof:
- (8) a compound represented by the structure:

$$R_2$$
 H
 ZR_1

a) Z is O or NH;

- b) R^1 is C_1 - C_6 alkyl, Ar^1 , or C_1 - C_4 alkoxycarbonylmethyl;
- c) X, Y, independently of one another, are H, Ar¹, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ haloalkyl, or halogen,

wherein said C₁-C₆ alkyl is optionally interrupted or substituted by heteroatoms selected from the group consisting of N, P, O, S and Si and said heteroatoms are optionally substituted by C₁-C₃ alkyl once or several times and

when X and Y are each carbon, they may be covalently joined to form a saturated or partially unsaturated cyclic compound of 3-8 members consisting independently of C, N, O, and S, further wherein ring members may themselves be unsubstituted or substituted with halo, hydroxyl, carboxy, nitro, trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁-C₄ alkenyloxy, phenoxy, benzyloxy, amino, substituted alkyl, Ar¹, or a combination thereof;

- d) R₂ is H, alkyl, Ar¹, or O substituted alkyl; and
- e) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro, trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁-C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the individual ring sizes are 3-7 members; and wherein the heterocyclic ring contains 1-6 heteroatom(s) selected from the group consisting of O, N, S, and any combination thereof;
- (9) a compound represented by the structure:

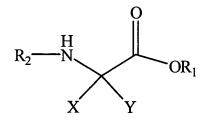
$$R_2$$
 N
 $*$
 OR_1
 X
 H

- a) * = asymmetric center;
- b) $R^1 = C_1 C_6$ alkyl, Ar^1 , or $C_1 C_4$ alkoxycarbonylmethyl;
- c) X is H, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ haloalkyl, halogen, or Ar¹, wherein said C₁-C₆ alkyl is optionally interrupted or substituted by heteroatoms selected from the group consisting of N, P, O, S and Si and said heteroatoms are optionally substituted by C₁-C₃ alkyl once or several times;
- d) R₂ is H, alkyl, Ar¹, or O substituted alkyl;
- e) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro, trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁-C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the individual ring sizes are 3-7 members; and wherein the heterocyclic ring contains 1-6 heteroatom(s) selected from the group consisting of O, N, S, and any combination thereof;
- (10) a compound represented by the structure:

$$R_2$$
 N
 OR_1

- a) X and Y are each carbon;
- b) X and Y are connected by a saturated or partially saturated ring of 3-8 carbons and such a ring may itself be substituted in one to five position(s) with halo, hydroxyl, carboxy, amino, nitro, cyano, trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁-C₄ alkenyloxy, or substituted alkyl groups;

- c) $R^1 = C_1 C_6$ alkyl, Ar^1 , or $C_1 C_4$ alkoxycarbonylmethyl;
- d) R₂ is H, alkyl, Ar¹, or O substituted alkyl; and
- e) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro, trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁-C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the individual ring sizes are 3-7 members; and wherein the heterocyclic ring contains 1-6 heteroatom(s) selected from the group consisting of O, N, S, and any combination thereof;
- (11) a compound represented by the structure:



- a) X, Y, independently of one another, are H, Ar¹, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ haloalkyl, or halogen, wherein said C₁-C₆ alkyl is optionally interrupted or substituted by heteroatoms selected from the group consisting of N, P, O, S and Si and said heteroatoms are optionally substituted by C₁-C₃ alkyl once or several times;
- b) R₂ is H, alkyl, Ar¹, or O substituted alkyl; and
- c) Ar¹ is a mono-, bi- or tricyclic, carbo- or heterocyclic ring, wherein the ring is either unsubstituted or substituted in one to three position(s) with halo, hydroxyl, nitro, trifluoromethyl, C₁-C₆ straight or branched chain alkyl or alkenyl, C₁-C₄ alkoxy, C₁-C₄ alkenyloxy, phenoxy, benzyloxy, amino, or a combination thereof; wherein the individual ring sizes are 3-7 members; and

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wherein the heterocyclic ring contains 1-6 heteroatom(s) selected from the group consisting of O, N, S, and any combination thereof; or

(12) a compound represented by the structure:

$$R_2$$
—NH O OR_1

or pharmaceutically acceptable salts thereof, wherein:

- a) $R^1 = C_1 C_6$ alkyl, Ar^1 , or $C_1 C_4$ alkoxycarbonylmethyl;
- b) R₂ is H, alkyl, Ar¹, or O substituted alkyl;
- c) Y is H, Ar¹, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₆ haloalkyl, or halogen, wherein said C₁-C₆ alkyl is optionally interrupted or substituted by heteroatoms selected from the group consisting of N, P, O, S and Si and said heteroatoms are optionally substituted by C₁-C₃ alkyl once or several times; and
- d) X is alkyl or phenyl.

31 (Previously Presented). The method according to claim 30, wherein said compound represented by the structure:

$$\begin{array}{c|c}
A & O \\
\hline
 & B & V
\end{array}$$

is cystathionine ketimine or cyclothionine.

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32 (Previously Presented). The method according to claim 30, wherein said compound represented by the structure:

is selected from the group consisting of: aminoethylcysteine-ketimine (2H-1,4-thiazine-5,6-dihydro-3-carboxylic acid), thiomorpholine-2-carboxylic acid, lanthionine ketimine, and 1,4-thiomorpholine-3, 5-dicarboxylic acid.

33-43 (canceled).

44 (new). The method according to claim 20, wherein said method determines whether said compound selectively reduces the enzymatic activity of said polypeptide.

45 (new). The method according to claim 20, wherein said method determines whether said compound selectively binds said polypeptide.